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Rifalazil treats and prevents relapse of clostridium difficile-associated diarrhea in hamsters

Anton, Pauline M; O'Brien, Michael; Kokkotou, Efi; Eisenstein, Barry; Michaelis, Arthur; Rothstein, David; Paraschos, Sophia; Kelly, Ciáran P; Pothoulakis, Charalabos

Beth Israel Deaconess Medical Center, Division of Gastroenterology, Dana 601, 330 Brookline Ave., Boston, MA 02215, USA; e-mail cpothoul@bidmc.harvard.edu

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Abstract

Although vancomycin and metronidazole effectively treat *Clostridium difficile*-associated diarrhea and colitis (CDAD), their use is associated with a high incidence of relapsing *C. difficile* infection. Rifalazil is a new benzoxazinorifamycin that possesses activity against *Mycobacterium tuberculosis* and gram-positive bacteria. Here we compared rifalazil and vancomycin for effectiveness in preventing or treating clindamycin-induced cecitis in a hamster model of CDAD. Golden Syrian hamsters were injected subcutaneously with clindamycin phosphate (10 mg/kg), followed 24 h later by *C. difficile* gavage. Hamsters received by gavage for 5 days vehicle, vancomycin (50 mg/kg), or rifalazil (20 mg/kg) either simultaneously with (**prophylactic protocol**) or 24 h after *C. difficile* administration (**treatment protocol**). While all vehicle-administered animals became moribund within 48 h of *C. difficile* administration, no rifalazil- or vancomycin-treated animals in either protocol showed signs of morbidity after 7 days. Ceca of rifalazil-treated animals showed absence of epithelial cell damage, significantly reduced congestion and edema, and less, but not statistically significantly less, neutrophil infiltration compared to those of vehicle-treated animals. In contrast, vancomycin-treated animals demonstrated severe epithelial cell damage and mildly reduced congestion and edema. Moreover, hamsters relapsed and tested *C. difficile* toxin positive (by enzyme-linked immunosorbent assay) 10 to 15 days after discontinuation of vancomycin treatment. None of the rifalazil-treated hamsters showed signs of disease or presence of toxins in their feces 30 days after discontinuation of treatment. Our results indicate that once daily rifalazil may be superior to vancomycin for curative treatment

of CDAD. [Journal Article; In English; United States]

CAS Registry Numbers: Anti-Bacterial Agents; Rifamycins; 129791-92-0, KRM 1648; 1404-90-6, Vancomycin

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